

## CLAIMS

What is claimed is:

1. A method of treating or preventing a central nervous system disorder, which comprises administering to a patient in need of such treatment or prevention a  
5 therapeutically or prophylactically effective amount of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

2. A method of managing a central nervous system disorder, which comprises administering to a patient in need of such management a prophylactically effective amount of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, or  
10 stereoisomer thereof.

3. The method of claim 1, wherein the central nervous system disorder is Parkinson disease; Alzheimer disease; mild cognitive impairment; Amyotrophic Lateral Sclerosis; CNS trauma; Alzheimer disease with parkinsonism; bradykinesia; akinesia; movement disorder that impairs fine motor control and finger dexterity; hypophonia;  
15 monotonic speech; rigidity; dystonia; inflammation associated with Parkinson disease; tremor of the face, jaw, tongue or posture; parkinsonian gait; shuffling; short step; festinating gait; disorder of mood, cognition, sensation, or sleep; dementia; depression; defective long-term memory; drug induced parkinsonism; vascular parkinsonism; multiple system atrophy; progressive supranuclear palsy; disorder with primary tau pathology;  
20 cortical basal ganglia degeneration; parkinsonism with dementia; hyperkinetic disorder; chorea; Huntington disease; dystonia; Wilson disease; Tourette syndrome; essential tremor; myoclonus; or a tardive movement disorder.

4. The method of claim 2, wherein the central nervous system disorder is Parkinson disease; Alzheimer disease; mild cognitive impairment; Amyotrophic Lateral  
25 Sclerosis; CNS trauma Alzheimer disease with parkinsonism; bradykinesia; akinesia; movement disorder that impairs fine motor control and finger dexterity; hypophonia; monotonic speech; rigidity; dystonia; inflammation associated with Parkinson disease; tremor of the face, jaw, tongue or posture; parkinsonian gait; shuffling; short step; festinating gait; disorder of mood, cognition, sensation, or sleep; dementia; depression;  
30 defective long-term memory; drug induced parkinsonism; vascular parkinsonism; multiple system atrophy; progressive supranuclear palsy; disorder with primary tau pathology;

cortical basal ganglia degeneration; parkinsonism with dementia; hyperkinetic disorder; chorea; Huntington disease; dystonia; Wilson disease; Tourette syndrome; essential tremor; myoclonus; or a tardive movement disorder.

5        5.        The method of claim 3, wherein the central nervous system disorder is  
5        Parkinson disease.

6.        The method of claim 4, wherein the central nervous system disorder is  
Parkinson disease.

7.        A method of treating or preventing a central nervous system disorder, which  
comprises administering to a patient in need of such treatment or prevention a  
10        therapeutically or prophylactically effective amount of a selective cytokine inhibitory drug,  
or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, and a therapeutically  
or prophylactically effective amount of at least one second active ingredient.

8.        A method of managing a central nervous system disorder, which comprises  
administering to a patient in need of such management a prophylactically effective amount  
15        of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, or  
stereoisomer thereof, and a therapeutically or prophylactically effective amount of at least  
one second active ingredient.

9.        The method of claim 7, wherein the central nervous system disorder is  
Parkinson disease.

20        10.       The method of claim 8, wherein the central nervous system disorder is  
Parkinson disease.

11.       The method of claim 7, wherein the second active ingredient is a dopamine  
agonist, a monoamine oxidase inhibitor (MAO), a catechol-O-methyltransferase inhibitor  
(COMT), amantadine, an acetylcholinesterase inhibitor, an antiemetic, or an  
25        anti-inflammatory agent.

12.       The method of claim 8, wherein the second active ingredient is a dopamine  
agonist, a monoamine oxidase inhibitor (MAO), a catechol-O-methyltransferase inhibitor  
(COMT), amantadine, an acetylcholinesterase inhibitor, an antiemetic, or an  
anti-inflammatory agent.

13. The method of any one of claims 1, 2, 7, or 8, wherein the stereoisomer of the selective cytokine inhibitory drug is an enantiomer.

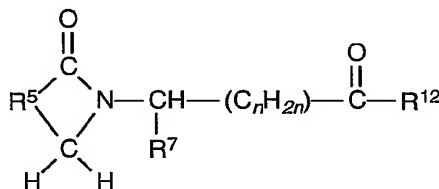
14. The method of any one of claims 1, 2, 7, or 8, wherein the selective cytokine inhibitory drug is 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl) propionamide.

15. The method of claim 14, wherein the selective cytokine inhibitory drug is the R or S enantiomer of 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl) propionamide.

16. The method of any one of claims 1, 2, 7 or 8, wherein the selective cytokine inhibitory drug is cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1 *H*-isoindol-4-yl}-amide.

17. The method of claim 16, wherein the selective cytokine inhibitory drug is the R or S enantiomer of cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1 *H*-isoindol-4-yl}-amide.

18. The method of any one of claims 1, 2, 7 or 8, wherein the selective cytokine inhibitory drug has formula (I):



(I)

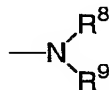
wherein n has a value of 1, 2, or 3;

R<sup>5</sup> is o-phenylene, unsubstituted or substituted with 1 to 4 substituents each selected independently from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxo, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, and halo;

R<sup>7</sup> is (i) phenyl or phenyl substituted with one or more substituents each selected independently of the other from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxo, carboxy, hydroxy, amino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, and halo, (ii) benzyl

unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, and halo, (iii) naphthyl, and (iv) benzyloxy;

5  $R^{12}$  is -OH, alkoxy of 1 to 12 carbon atoms, or

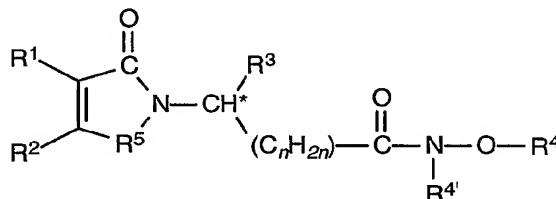


$R^8$  is hydrogen or alkyl of 1 to 10 carbon atoms; and

$R^9$  is hydrogen, alkyl of 1 to 10 carbon atoms,  $-\text{COR}^{10}$ , or  $-\text{SO}_2\text{R}^{10}$ , wherein  $R^{10}$  is hydrogen, alkyl of 1 to 10 carbon atoms, or phenyl.

10 19. The method of claim 18, wherein the selective cytokine inhibitory drug is an enantiomer of the compound having formula (I).

20. The method of any one of claims 1, 2, 7 or 8, wherein the selective cytokine inhibitory drug has formula (II):



15 (II)

wherein each of  $R^1$  and  $R^2$ , when taken independently of each other, is hydrogen, lower alkyl, or  $R^1$  and  $R^2$ , when taken together with the depicted carbon atoms to which each is bound, is *o*-phenylene, *o*-naphthylene, or cyclohexene-1,2-diyl, unsubstituted or substituted with 1 to 4 substituents each selected independently from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, and halo;

$R^3$  is phenyl substituted with from one to four substituents selected from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, alkylthio of 1 to 10 carbon atoms, benzyloxy, cycloalkoxy of 3 to 6

carbon atoms, C<sub>4</sub>-C<sub>6</sub>-cycloalkyldenemethyl, C<sub>3</sub>-C<sub>10</sub>-alkyldenemethyl, indanyloxy, and halo;

R<sup>4</sup> is hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, or benzyl;

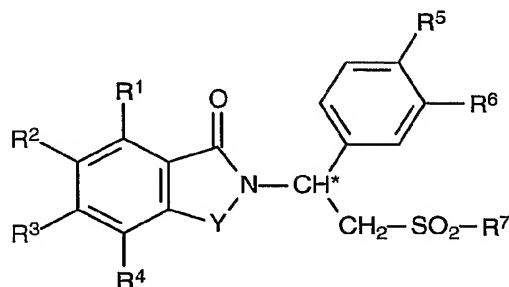
R<sup>4'</sup> is hydrogen or alkyl of 1 to 6 carbon atoms;

5 R<sup>5</sup> is -CH<sub>2</sub>-, -CH<sub>2</sub>-CO-, -SO<sub>2</sub>-, -S-, or -NHCO-; and

n has a value of 0, 1, or 2.

21. The method of claim 20, wherein the selective cytokine inhibitory drug is an enantiomer of the compound having formula (II).

22. The method of any one of claims 1, 2, 7 or 8, wherein the selective cytokine  
10 inhibitory drug has formula (III):



(III)

wherein the carbon atom designated \* constitutes a center of chirality;

Y is C=O, CH<sub>2</sub>, SO<sub>2</sub>, or CH<sub>2</sub>C=O;

15 each of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup>, independently of the others, is hydrogen, halo, alkyl of 1 to 4 carbon atoms, alkoxy of 1 to 4 carbon atoms, nitro, cyano, hydroxy, or -NR<sup>8</sup>R<sup>9</sup>; or any two of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> on adjacent carbon atoms, together with the depicted phenylene ring are naphthylidene;

20 each of R<sup>5</sup> and R<sup>6</sup>, independently of the other, is hydrogen, alkyl of 1 to 4 carbon atoms, alkoxy of 1 to 4 carbon atoms, cyano, or cycloalkoxy of up to 18 carbon atoms;

R<sup>7</sup> is hydroxy, alkyl of 1 to 8 carbon atoms, phenyl, benzyl, or NR<sup>8</sup>R<sup>9</sup>;

25 each of R<sup>8</sup> and R<sup>9</sup> taken independently of the other is hydrogen, alkyl of 1 to 8 carbon atoms, phenyl, or benzyl, or one of R<sup>8</sup> and R<sup>9</sup> is hydrogen and the other is -COR<sup>10</sup> or -SO<sub>2</sub>R<sup>10</sup>, or R<sup>8</sup> and R<sup>9</sup> taken together are tetramethylene, pentamethylene, hexamethylene, or -CH<sub>2</sub>CH<sub>2</sub>X<sup>1</sup>CH<sub>2</sub>CH<sub>2</sub>- in which X<sup>1</sup> is -O-, -S- or -NH-; and

each of R<sup>8'</sup> and R<sup>9'</sup> taken independently of the other is hydrogen, alkyl of 1 to 8 carbon atoms, phenyl, or benzyl, or one of R<sup>8'</sup> and R<sup>9'</sup> is hydrogen and the other is -COR<sup>10'</sup>

or  $-\text{SO}_2\text{R}^{10'}$ , or  $\text{R}^{8'}$  and  $\text{R}^{9'}$  taken together are tetramethylene, pentamethylene, hexamethylene, or  $-\text{CH}_2\text{CH}_2\text{X}^2\text{CH}_2\text{CH}_2-$  in which  $\text{X}^2$  is  $-\text{O}-$ ,  $-\text{S}-$ , or  $-\text{NH}-$ .

23. The method of claim 22, wherein the selective cytokine inhibitory drug is an enantiomer of said compound.

5           24. A method of reducing or avoiding an adverse effect associated with the administration of a second active ingredient in a patient suffering from a central nervous system disorder, which comprises administering to a patient in need of such reduction or avoidance an amount of the second active ingredient and a therapeutically or prophylactically effective amount of a selective cytokine inhibitory drug, or a  
10           pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

25. A pharmaceutical composition comprising a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, or stereoisomer, thereof in an amount effective to treat, prevent or manage a central nervous system disorder, and a carrier.

26. A pharmaceutical composition comprising a selective cytokine inhibitory  
15           drug, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, in an amount effective to treat, prevent or manage a central nervous system disorder, and a second active ingredient.

27. The pharmaceutical composition of claim 26, wherein the second active  
ingredient is a dopamine agonist, a monoamine oxidase inhibitor (MAO), a  
20           catechol-O-methyltransferase inhibitor (COMT), amantadine, an anticholinergic, an antiemetic, or an anti-inflammatory agent.